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Comparing patch test results of methylchloroisothiazolinone/methylisothiazolinone tested with both TRUE Test® and 100 ppm using investigator-loaded chambers

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Key words: allergic contact dermatitis; methychloroisothiazolinone; methylisothiazolinone; patch test; TRUE Test®.

Methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI), a widely used preservative/biocide, was included in the European baseline series in 1988 at a concentration of 100 ppm (0.01%) in a ratio of 3:1 (1). Although recently it has been recommended to be tested at 200 ppm (0.02%), many centres still test it at 100 ppm (2). MCI/MI is also included in the TRUE Test®, offering an alternative patch test technique. The objective of the current investigation was to compare the diagnostic performance of MCI/MI 0.01% aq. with MCI/MI in the TRUE Test®.

Methods

Between April 2013 and August 2016, a total of 1122 consecutive patients were patch tested with our departmental baseline series, of whom 1115 (99.4%) were tested simultaneously with both MCI/MI 4 μg/cm^2 (TRUE Test®; Mekos, Hillerød, Denmark) and MCI/MI 0.01% aq. (Trolab; Almirall Hermal, Reinbek, Germany), corresponding to a dose per unit area of 3 μg/cm^2, in Van der Bend® square chambers (van der Bend, Brielle, The Netherlands), attached to the back with Fixomull stretch® (BSN Medical, Hamburg, Germany). Twenty microlitres of the aqueous solution of MCI/MI was applied to the chambers with a micropipette. The patch tests were applied on the back for 48 h under occlusion, and readings were performed on day (D) 3 and D7 according to ESCD guidelines (3). The maximum patch test reactions were aggregated as the patch test outcome. In case of a positive reaction (+, ++, or +++), clinical relevance was determined on basis of patient history, clinical examination, and exposure patterns, with possible outcomes being unlikely/not, possible, probable, and certain. Statistical analyses were performed with SPSS (version 23.0; SPSS, Chicago, IL, USA), and guidelines for contact allergy data were followed (4). The McNemar test was used to compare the strength of reactions of both patch test preparations.

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Results

The MOAHLFA index for the investigated patient group was as follows: male, 32.6%; occupational dermatitis, 24.1%; atopic dermatitis, 40.9%; hand, 34.0%; leg, 22.4%; face, 3.7%; and age $\geq$ 40 years, 57.5%. A total of 14.4% (n = 161) of patients had a positive reaction to one of the MCI/MI preparations; 13.6% (95%CI: 11.6–15.6%) had positive reactions to MCI/MI TRUE Test®, and 7.2% (95%CI: 5.7–8.7%) had positive reactions to MCI/MI 3 μg/cm^2 aq. The patch test reactions to MCI/MI TRUE Test® were significantly stronger ($p < 0.001$). Table 1 shows the patterns of reactions to both patch test preparations in greater detail. Of all patients with positive reactions to MCI/MI TRUE Test® (n = 152), 81 (53.3%) did not have positive reactions to MCI/MI 3 μg/cm^2 aq. Furthermore, 35 of these 81 reactions were strong to extreme positive reactions. Conversely, of the 80 patients who had positive reactions to MCI/MI 3 μg/cm^2 aq., 9 (11.3%) did not react to MCI/MI TRUE Test®.

The clinical relevance of all positive reactions was determined, and is shown in Table 2. Of all positive reactions to MCI/MI TRUE Test®, 88.8% (135/152) had some

Table 1. Relationship between patch test reactions of methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) TRUE Test® and MCI/MI 0.01% aq.

		MCI/MI 0.01% aq.						
		Negative	Irritant	Doubtful	+	++	+++	Total
MCI/MI TRUE Test®	Negative	931	2	14	8	1	0	956
	Irritant	1	0	0	0	0	0	1
	Doubtful	5	0	1	0	0	0	6
	+	37	0	9	15	1	0	62
	++	27	0	2	29	16	0	74
	+++	6	0	0	4	5	1	16
Total		1007	2	26	56	23	1	1115

Table 2. The clinical relevance of all positive reactions to either methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) TRUE Test® or MCI/MI 0.01% aq.

Clinical relevance	% (n) of patients with a positive reaction to MCI/MI TRUE Test® (n = 152)	% (n) of patients with a positive reaction to MCI/MI 0.01% aq. (n = 80)
Unlikely/not	7.2 (11)	11.3 (9)
Unknown	4.0 (6)	1.3 (1)
Possible	38.8 (59)	32.5 (26)
Probable	27.0 (41)	23.8 (19)
Certain	23.0 (35)	31.3 (25)

degree of clinical relevance (ranging from possible to certain), as compared with 87.5% (70/80) of positive reactions to MCI/MI 3 μg/cm^2 aq. For the 9 patients with positive reactions to MCI/MI 3 μg/cm^2 aq. but without positive reactions to MCI/MI TRUE Test®, six reactions were considered to be of possible clinical relevance, two of probable clinical relevance, and one of no clinical relevance. Conversely, for the 81 patients with positive reactions to MCI/MI TRUE Test® but without positive reactions to MCI/MI 3 μg/cm^2 aq., 90.1% (n = 73) of reactions had some degree of clinical relevance (39 possible, 24 probable, and 10 certain), three reactions were of unknown clinical relevance, and the remaining five were of no clinical relevance. This means that, if this cohort had been patch tested solely with MCI/MI 3 μg/cm^2 aq., there would have been 73 missed reactions, constituting 6.5% of all consecutively patch tested patients.

Discussion

Although the prevalence of MCI/MI contact allergy in patch test populations remained relatively stable at 2.5% for a long period of time, recent publications have shown it to be rapidly rising (5–8). The most recent publication of the European Surveillance System on Contact Allergies (ESSCA) showed a standardized prevalence of 7.3% for contact allergy to MCI/MI 0.01% in 2013–2014, which is similar to our results (9).

More surprising in the current results is the high proportion of positive reactions to the TRUE Test® preparation, which was almost twice as high, at 13.6%. A large majority of these positive reactions were deemed to have at least some degree of clinical relevance, making the possibility of false positives less likely. The concentration of MCI/MI in the TRUE Test®, at 4 μg/cm^2, is slightly higher than the 3 μg/cm^2 of MCI/MI 0.01% aq., which explains part of this discrepancy, as MCI/MI has a steep dose–response curve (7). This also illustrates that, besides dose, other factors, such as vehicle, also affect elicitation responses, as MCI/MI is tested in povidone in the TRUE Test® (10). A major limitation of the current study is that MCI/MI was not tested at a concentration of 0.02% (200 ppm or 6 μg/cm^2), which would have allowed an even better comparison of the different patch test techniques, but this might be addressed by future studies.

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